In the Claims

Please cancel claims 1-122 without prejudice to applicants' right to pursue the subject matter of these claims in a future continuing application and add new claims 123-164 as follows:

1-122. (Canceled)

123. (New) In a process for obtaining a pharmaceutical product containing an aqueous mixture of polypeptides, each of which consists essentially of alanine, glutamic acid, tyrosine and lysine, wherein the mixture has a desired average molecular weight and wherein during the process a batch of an aqueous mixture of polypeptides, each of which consists essentially of alanine, glutamic acid, tyrosine and lysine, is tested using a gel permeation chromatography column to determine whether the mixture has the desired average molecular weight for inclusion in the pharmaceutical product, the improvement comprising

calibrating the molecular weight obtained using the gel permeation chromatography column by subjecting a plurality of molecular weight markers, each of which is a polypeptide consisting essentially of alanine, glutamic acid, tyrosine and lysine and having a predetermined amino acid sequence, to chromatography on the column to establish a relationship between retention time on the column and molecular weight.

124. (New) The process of claim 123, wherein the mixture of polypeptide that is tested is glatiramer acetate.

125. (New) The process of claim 124, wherein the glatiramer acetate has an average molecular weight from 4000 to 13,000 Daltons.

126. (New) The process of claim 125, wherein in the glatiramer acetate the molar fraction of analine is 0.427, of glutamic acid is 0.141, of lysine is 0.337 and of tyrosine is 0.093.

127. (New) The process of claim 123, wherein the gel permeation chromatography column comprises a cross-linked agarose-based medium, with an exclusion limit of 2×10^6 Daltons, an optimal separation range of 1000 to 3×10^5 Daltons, and a bead diameter of 20-40 μm.

128. (New) The process of claim 127, wherein the gel permeation chromatography column is Superose 12.

129. (New) The process of claim 123, wherein in the molecular weight markers the molar fraction of analine is 0.38 to 0.5, of glutamic acid is 0.13 to 0.15, of tyrosine is 0.08 to 0.10 and of lysine is 0.3 to 0.4.

130. (New) The process of claim 129, wherein in the molecular weight markers the molar fraction of analine is 0.422 to 0.444, of glutamic acid is 0.133 to 0.143, of tyrosine is 0.086 to 0.093 and of lysine is 0.333 to 0.349.

131. (New) The process of claim 123, wherein one of the molecular weight markers is selected from the group consisting of

AKKYAKKEKAAKKAYKKEAKAKAAEAAAKEAAYEA (SEQ ID NO:1);
AKKYAKKAKAEKAKKAYKAAEAKKAAKYEKAAAEKAAAKEAAYEA (SEQ ID NO:2);
AKKYAKKEKAYAKKAEKAAKKAEAKAYKAAEAKKKAEAKYKAEAAKAAAKEAAYEA (SEQ ID NO:3);
AKKYAKKEKAYAKAKKAEAKAAKKAKAEAKKYAKAAKAEKKEYAAAEAKYKAEAAKAAAKEAAYEA (SEQ ID NO:4);
AKKYAKKEKAYAKKAEKAAKKAEAKAYKAAEAKKKAKAEAKKYAKAAKAEKKEYAAAEAKYKAEAAKAAAKEAAYEA (SEQ ID NO:5);
AKKYAKKEKAYAKKAEKAAKKAEAKAYKAAEAKKKAKAEAKKYAKAAKAEKKEYAAAEAKYKAEAAKKAYKAEAAKAAAKEAAYEA (SEQ ID NO:6); and
AKKYAKKAEKAYAKKAKAAKEKKAYAKKEAKAYKAAEAKKKAKAEAKKYAKEAAKAKKEAYKAEAKKYAKAAKAEKKEYAAAEAKKAEAAKAYKAEAAKAAAKEAAYEA (SEQ ID NO:7),

wherein A represents alanine, K represents lysine, Y represents tyrosine, and E represents glutamic acid.

132. (New) The process of claim 123, wherein the plurality of molecular weight markers is

AKKYAKKEKAAKKAYKKEAKAKAAEAAAKEAAYEA (SEQ ID NO:1);
AKKYAKKAKAEKAKKAYKAAEAKKAAKYEKAAAEKAAAKEAAYEA (SEQ ID NO:2);
AKKYAKKEKAYAKKAEKAAKKAEAKAYKAAEAKKKAEAKYKAEAAKAAAKEAAYEA (SEQ ID NO:3);
AKKYAKKEKAYAKAKKAEAKAAKKAKAEAKKYAKAAKAEKKEYAAAEAKYKAEAAKAAAKEAAYEA (SEQ ID NO:4);
AKKYAKKEKAYAKKAEKAAKKAEAKAYKAAEAKKKAKAEAKKYAKAAKAEKKEYAAAEAKYKAEAAKAAAKEAAYEA (SEQ ID NO:5);

AKKYAKKEKAYAKKAEKAAKKAEAKAYKAAEAKKKAKAEAKKYAKAAKAEKKEYA AAEAKYKAEAAKKAYKAEAAKAAAKEAAYEA (SEQ ID NO:6); and AKKYAKKAEKAYAKKAKAAKEKKAYAKKEAKAYKAAEAKKKAKAEAKKYAKEAAK AKKEAYKAEAKKYAKAAKAEKKEYAAAEAKKAEAAKAYKAEAAKAAAKEAAYEA (SEQ ID NO:7),

wherein A represents alanine, K represents lysine, Y represents tyrosine, and E represents glutamic acid.

133. (New) The process of claim 124, further comprising a step of lyophilizing of the glatiramer acetate.

134. (New) A process for obtaining a pharmaceutical composition containing an aqueous mixture of polypeptides, each of which consists essentially of alanine, glutamic acid, tyrosine and lysine, wherein the mixture has a desired average molecular weight, which comprises obtaining a batch of an aqueous mixture of polypeptides, each of which consists essentially of alanine, glutamic acid, tyrosine and lysine;

determining the average molecular weight of the mixture of polypeptides in the batch using a molecular weight-calibrated gel permeation chromatography column; and

including in the pharmaceutical product the mixture if the mixture is determined to have the desired average molecular weight,

wherein the calibration of the molecular weight obtained using the gel permeation chromatography column comprises subjecting a plurality of molecular weight markers to chromatography on the column to establish a relationship between the retention time on the column

and molecular weight, wherein each of the markers is a polypeptide consisting essentially of alanine, glutamic acid, tyrosine and lysine and has a predetermined amino sequence.

135. (New) The process of claim 134, wherein the batch of the aqueous mixture of polypeptide is glatiramer acetate.

136. (New) The process of claim 135, wherein the glatiramer acetate has an average molecular weight from 4000 to 13,000 Daltons.

137. (New) The process of claim 136, wherein in the glatiramer acetate the molar fraction of analine is 0.427, of glutamic acid is 0.141, of lysine is 0.337 and of tyrosine is 0.093.

138. (New) The process of claim 134, wherein the gel permeation chromatography column comprises a cross-linked agarose-based medium, with an exclusion limit of 2×10^6 Daltons, an optimal separation range of 1000 to $3x\ 10^5$ Daltons, and a bead diameter of 20-40 µm.

139. (New) The process of claim 138, wherein the gel permeation chromatography column is Superose 12.

140. (New) The process of claim 134, wherein in the molecular weight markers the molar fraction of analine is 0.38 to 0.5, of glutamic acid is 0.13 to 0.15, of tyrosine is 0.08 to 0.10 and of lysine is 0.3 to 0.4.

141. (New) The process of claim 140, wherein in the molecular weight markers the molar fraction of analine is 0.422 to 0.444, of glutamic acid is 0.133 to 0.143, of tyrosine is 0.086 to 0.093 and of lysine is 0.333 to 0.349.

142. (New) The process of claim 134, wherein one of the molecular weight markers is selected from the group consisting of

AKKYAKKEKAAKKAYKKEAKAKAAEAAAKEAAYEA (SEQ ID NO:1);
AKKYAKKAKAEKAKKAYKAAEAKKAAKYEKAAAEKAAAKEAAYEA (SEQ ID NO:2);
AKKYAKKEKAYAKKAEKAAKKAEAKAYKAAEAKKKAEAKYKAEAAKAAAKEAAYEA (SEQ ID NO:3);
AKKYAKKEKAYAKAKKAEAKAAKKAKAEAKKYAKAAKAEKKEYAAAEAKYKAEAAKAAAKEAAYEA (SEQ ID NO:4);
AKKYAKKEKAYAKKAEKAAKKAEAKAYKAAEAKKKAKAEAKKYAKAAKAEKKEYAAAEAKYKAEAAKAAAKEAAYEA (SEQ ID NO:5);
AKKYAKKEKAYAKKAEKAAKKAEAKAYKAAEAKKKAKAEAKKYAKAAKAEKKEYAAAEAKYKAEAAKKAYKAEAAKAAAKEAAYEA (SEQ ID NO:6); and
AKKYAKKAEKAYAKKAKAAKEKKAYAKKEAKAYKAAEAKKKAKAEAKKYAKEAAKAKKEAYKAEAKKYAKAAKAEKKEYAAAEAKKAEAAKAYKAEAAKAAAKEAAYEA (SEQ ID NO:7),

wherein A represents alanine, K represents lysine, Y represents tyrosine, and E represents glutamic acid.

143. (New) The process of claim 134, wherein the plurality of molecular weight markers is

AKKYAKKEKAAKKAYKKEAKAKAAEAAAKEAAYEA (SEQ ID NO:1);

AKKYAKKAKAEKAKKAYKAAEAKKAAKYEKAAAEKAAAKEAAYEA (SEQ ID NO:2);

AKKYAKKEKAYAKKAEKAAKKAEAKAYKAAEAKKKAEAKYKAEAAKAAAKEAAYEA (SEQ ID NO:3);

AKKYAKKEKAYAKAKKAEAKAAKKAKAEAKKYAKAAKAEKKEYAAAEAKYKAEAAKAAAKEAAYEA (SEQ ID NO:4);

AKKYAKKEKAYAKKAEKAAKKAEAKAYKAAEAKKKAKAEAKKYAKAAKAEKKEYAAAEAKYKAEAAKAAAKEAAYEA (SEQ ID NO:5);

AKKYAKKEKAYAKKAEKAAKKAEAKAYKAAEAKKKAKAEAKKYAKAAKAEKKEYAAAEAKYKAEAAKKAYKAEAAKAAAKEAAYEA (SEQ ID NO:6); and

AKKYAKKAEKAYAKKAKAAKEKKAYAKKEAKAYKAAEAKKKAKAEAKKYAKEAAKAKKEAYKAEAKKYAKAAKAEKKEYAAAEAKKAEAAKAYKAEAAKAAAKEAAYEA (SEQ ID NO:7),

wherein A represents alanine, K represents lysine, Y represents tyrosine, and E represents glutamic acid.

144. (New) The process of claim 135, further comprising a step of lyophilizing of the glatiramer acetate having the desired average molecular weight distribution.

145. (New) A process for determining the average molecular weight of an aqueous mixture of polypeptides, each of which consists essentially of alanine, glutamic acid, tyrosine and lysine, which comprises subjecting the mixture to chromatography on a molecular weight-calibrated gel permeation chromatography column so as to determine the average molecular weight of the mixture, wherein the calibration of the molecular weight obtained using the gel permeation chromatography column comprises subjecting a plurality of molecular weight markers to chromatography on the column to

establish a relationship between retention time on the column and molecular weight, wherein each of the markers is a polypeptide consisting essentially of alanine, glutamic acid, tyrosine and lysine and has a predetermined amino acid sequence.

146. (New) The process of claim 145, wherein the aqueous mixture of polypeptide is glatiramer acetate.

147. (New) The process of claim 146, wherein the glatiramer acetate has an average molecular weight from 4000 to 13,000 Daltons.

148. (New) The process of claim 147, wherein in the glatiramer acetate the molar fraction of analine is 0.427, of glutamic acid is 0.141, of lysine is 0.337 and of tyrosine is 0.093.

149. (New) The process of claim 145, wherein the gel permeation chromatography column comprises a cross-linked agarose-based medium, with an exclusion limit of 2×10^6 Daltons, an optimal separation range of 1000 to $3x\ 10^5$ Daltons, and a bead diameter of 20-40 μm.

150. (New) The process of claim 149, wherein the gel permeation chromatography column is Superose 12.

151. (New) The process of claim 145, wherein in the molecular weight markers the molar fraction of analine is 0.38 to 0.5, of glutamic acid is 0.13 to 0.15, of tyrosine is 0.08 to 0.10 and of lysine is 0.3 to 0.4.

152. (New) The process of claim 151, wherein in the molecular weight markers the molar fraction of analine is 0.422 to 0.444, of glutamic acid is 0.133 to 0.143, of tyrosine is 0.086 to 0.093 and of lysine is 0.333 to 0.349.

153. (New) The process of claim 145, wherein one of the molecular weight markers is selected from the group consisting of

AKKYAKKEKAAKKAYKKEAKAKAAEAAAKEAAYEA (SEQ ID NO:1);
AKKYAKKAKAEKAKKAYKAAEAKKAAKYEKAAAEKAAAKEAAYEA (SEQ ID NO:2);
AKKYAKKEKAYAKKAEKAAKKAEAKAYKAAEAKKKAEAKYKAEAAKAAAKEAAYEA (SEQ ID NO:3);
AKKYAKKEKAYAKAKKAEAKAAKKAKAEAKKYAKAAKAEKKEYAAAEAKYKAEAAKAAAKEAAYEA (SEQ ID NO:4);
AKKYAKKEKAYAKKAEKAAKKAEAKAYKAAEAKKKAKAEAKKYAKAAKAEKKEYAAAEAKYKAEAAKAAAKEAAYEA (SEQ ID NO:5);
AKKYAKKEKAYAKKAEKAAKKAEAKAYKAAEAKKKAKAEAKKYAKAAKAEKKEYAAAEAKYKAEAAKKAYKAEAAKAAAKEAAYEA (SEQ ID NO:6); and
AKKYAKKAEKAYAKKAKAAKEKKAYAKKEAKAYKAAEAKKKAKAEAKKYAKEAAKAKKEAYKAEAKKYAKAAKAEKKEYAAAEAKKAEAAKAYKAEAAKAAAKEAAYEA (SEQ ID NO:7),

wherein A represents alanine, K represents lysine, Y represents tyrosine, and E represents glutamic acid.

154. (New) The process of claim 145, wherein the plurality of molecular weight markers is

AKKYAKKEKAAKKAYKKEAKAKAAEAAAKEAAYEA (SEQ ID NO:1);

AKKYAKKAKAEKAKKAYKAAEAKKAAKYEKAAAEKAAAKEAAYEA (SEQ ID NO:2);

AKKYAKKEKAYAKKAEKAAKKAEAKAYKAAEAKKKAEAKYKAEAAKAAAKEAAYEA (SEQ ID NO:3);

AKKYAKKEKAYAKAKKAEAKAAKKAKAEAKKYAKAAKAEKKEYAAAEAKYKAEAAKAAAKEAAYEA (SEQ ID NO:4);

AKKYAKKEKAYAKKAEKAAKKAEAKAYKAAEAKKKAKAEAKKYAKAAKAEKKEYAAAEAKYKAEAAKAAAKEAAYEA (SEQ ID NO:5);

AKKYAKKEKAYAKKAEKAAKKAEAKAYKAAEAKKKAKAEAKKYAKAAKAEKKEYAAAEAKYKAEAAKKAYKAEAAKAAAKEAAYEA (SEQ ID NO:6); and

AKKYAKKAEKAYAKKAKAAKEKKAYAKKEAKAYKAAEAKKKAKAEAKKYAKEAAKAKKEAYKAEAKKYAKAAKAEKKEYAAAEAKKAEAAKAYKAEAAKAAAKEAAYEA (SEQ ID NO:7),

wherein A represents alanine, K represents lysine, Y represents tyrosine, and E represents glutamic acid.

155. (New) A process for determining whether an aqueous mixture of polypeptides, each of which consists essentially of alanine, glutamic acid, tyrosine and lysine, has a desired average molecular weight, which comprises subjecting the mixture to a calibrated gel permeation chromatography column to determine the average molecular weight of the mixture and comparing the average molecular weight so determined to the desired average molecular weight, wherein the calibration of the molecular weight obtained using the gel permeation chromatography column comprises subjecting a plurality of molecular weight markers to chromatography on the column to establish a relationship between retention time on the column and molecular weight, wherein, each of the markers is a

polypeptide consisting essentially of alanine, glutamic acid, tyrosine and lysine and has a predetermined amino acid sequence.

156. (New) The process of claim 155, wherein the mixture of polypeptide that is tested is glatiramer acetate.

157. (New) The process of claim 156, wherein the glatiramer acetate has an average molecular weight from 4000 to 13,000 Daltons.

158. (New) The process of claim 157, wherein in the glatiramer acetate the molar fraction of analine is 0.427, of glutamic acid is 0.141, of lysine is 0.337 and of tyrosine is 0.093.

159. (New) The process of claim 155, wherein the gel permeation chromatography column comprises a cross-linked agarose-based medium, with an exclusion limit of 2×10^6 Daltons, an optimal separation range of 1000 to $3x\ 10^5$ Daltons, and a bead diameter of 20-40 μm.

160. (New) The process of claim 159, wherein the gel permeation chromatography column is Superose 12.

161. (New) The process of claim 155, wherein in the molecular weight markers the molar fraction of analine is 0.38 to 0.5, of glutamic acid is 0.13 to 0.15, of tyrosine is 0.08 to 0.10 and of lysine is 0.3 to 0.4.

162. (New) The process of claim 161, wherein in the molecular weight markers the molar fraction of analine

is 0.422 to 0.444, of glutamic acid is 0.133 to 0.143, of tyrosine is 0.086 to 0.093 and of lysine is 0.333 to 0.349.

163. (New) The process of claim 155, wherein one of the molecular weight markers is selected from the group consisting of

AKKYAKKEKAAKKAYKKEAKAKAAEAAAKEAAYEA (SEQ ID NO:1);
AKKYAKKAKAEKAKKAYKAAEAKKAAKYEKAAAEKAAAKEAAYEA (SEQ ID NO:2);
AKKYAKKEKAYAKKAEKAAKKAEAKAYKAAEAKKKAEAKYKAEAAKAAAKEAAYEA (SEQ ID NO:3);
AKKYAKKEKAYAKAKKAEAKAAKKAKAEAKKYAKAAKAEKKEYAAAEAKYKAEAAKAAAKEAAYEA (SEQ ID NO:4);
AKKYAKKEKAYAKKAEKAAKKAEAKAYKAAEAKKKAKAEAKKYAKAAKAEKKEYAAAEAKYKAEAAKAAAKEAAYEA (SEQ ID NO:5);
AKKYAKKEKAYAKKAEKAAKKAEAKAYKAAEAKKKAKAEAKKYAKAAKAEKKEYAAAEAKYKAEAAKKAYKAEAAKAAAKEAAYEA (SEQ ID NO:6); and
AKKYAKKAEKAYAKKAKAAKEKKAYAKKEAKAYKAAEAKKKAKAEAKKYAKEAAKAKKEAYKAEAKKYAKAAKAEKKEYAAAEAKKAEAAKAYKAEAAKAAAKEAAYEA (SEQ ID NO:7),

wherein A represents alanine, K represents lysine, Y represents tyrosine, and E represents glutamic acid.

164. (New) The process of claim 155, wherein the plurality of molecular weight markers is

AKKYAKKEKAAKKAYKKEAKAKAAEAAAKEAAYEA (SEQ ID NO:1);
AKKYAKKAKAEKAKKAYKAAEAKKAAKYEKAAAEKAAAKEAAYEA (SEQ ID NO:2);

AKKYAKKEKAYAKKAEKAAKKAEAKAYKAAEAKKKAEAKYKAEAAKAAAKEAAYE A (SEQ ID NO:3);

AKKYAKKEKAYAKAKKAEAKAAKKAKAEAKKYAKAAKAEKKEYAAAEAKYKAEAA KAAAKEAAYEA (SEQ ID NO:4);

AKKYAKKEKAYAKKAEKAAKKAEAKAYKAAEAKKKAKAEAKKYAKAAKAEKKEYA AAEAKYKAEAAKAAAKEAAYEA (SEQ ID NO:5);

AKKYAKKEKAYAKKAEKAAKKAEAKAYKAAEAKKKAKAEAKKYAKAAKAEKKEYA AAEAKYKAEAAKKAYKAEAAKAAAKEAAYEA (SEQ ID NO:6); and

AKKYAKKAEKAYAKKAKAAKEKKAYAKKEAKAYKAAEAKKKAKAEAKKYAKEAAK AKKEAYKAEAKKYAKAAKAEKKEYAAAEAKKAEAAKAYKAEAAKAAAKEAAYEA (SEQ ID NO:7),

wherein A represents alanine, K represents lysine, Y represents tyrosine, and E represents glutamic acid.